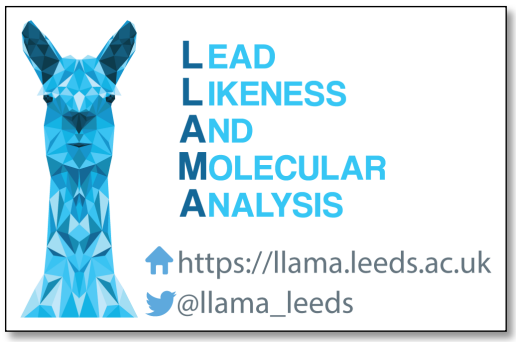
Lead-Oriented Synthesis: Exploring Drug-Relevant Chemical Diversity

GSK, 25 September 2015

Lead-Oriented Synthesis: Exploring Drug-Relevant Chemical Diversity was a one-day meeting organized by the Dial-a-Molecule Grand Challenge Network, and held at GlaxoSmithKline's Stevenage site on September 25, 2015. The meeting attracted 92 registered delegates, and featured **scientific talks** from academic and industrial leaders in the field. It also coincided with the launch of the open access software package **LLAMA** (Lead-Likeness And Molecule Analysis), developed at the University of Leeds.



Dr Ian Churcher (GSK) kicked off the meeting and set the scene for the remaining talks with a personal account of "*How Synthetic Chemistry Can Drive the Discovery of Drugs of the Future*", and concluding with the message that "synthesis is not a mature science and still needs to grow". This was followed by **Prof. Peter O'Brien** (University of York) who began his talk "*Exploring 3-D Pharmaceutical Space: Lead-oriented and Fragment-oriented Synthesis*" by introducing the growing interest in "moving away from flat-land", before discussing the progress his group has made in this area by utilizing organo-lithium chemistry.

After the lunch break, **Prof. Steve Marsden** (University of Leeds) spoke on "*Synthetic Strategies for the Efficient Exploration of Lead-Like Space*" and provided some recent examples from his group. **Dr Jason Kettle** (AstraZeneca) followed with "*Design and Exploitation of Novel Medicinal Chemistry Reagent Sets*", which explained some of the concepts used by industry to gain access to novel building blocks. The session was concluded with **Prof. David Spring** (University of Cambridge) who talked about "*Enriching Chemical Space to Drug Undruggable Targets*" and the work his group is carrying out with PPI's.

The day concluded with a Plenary Lecture from **Prof. Jeffrey Bode** (*ETHZ*) on "*Cross-Coupling 2.0*", where he gave an excellent account of both the SNAP and SLAP "Click" reagents developed in his group, and the KAT and KAHA ligation reactions they have developed to synthesize large peptides and proteins.

Alongside these excellent scientific presentations, the meeting involved also coincided with the launch of the **LLAMA** (Lead Likeness And Molecule Analysis), an open access, free to use tool which allows the lead-likeness of different molecular scaffolds to be evaluated and compared. The tool was developed at The University of Leeds as part of an EPSRC-funded collaboration with GSK. **Dr Richard Doveston** (*TU Eindhoven*) and **Prof Adam Nelson** (*University of Leeds*)

gave a brief introduction to software and over the lunch and refreshment breaks delegates got the chance to try the software and assess the lead-likeness of their own molecules.

Overall, the meeting was a huge success and enjoyed by all. The quality of the chemistry that was spoken about, and demonstrated over the lunch breaks, was truly innovative and at the forefront of synthetic developments, really emphasizing the point made in the opening session that synthesis is not a mature science and still needs to grow.